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BUREAU OF COMMUNICABLE DISEASE CONTROL

To: Health Care Providers  
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Subject: Toxigenic diphtheria cultured from a patient with respiratory symptoms

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**Patient with Toxigenic Diphtheria and Respiratory Symptoms**

On October 12, 2004, the Massachusetts Department of Public Health (MDPH) confirmed that *Corynebacterium diphtheriae* had been cultured from a throat swab taken from a 60-year-old Haitian-born woman, with an unknown vaccination status, who had been living in the United States for 18 years, and had not visited Haiti since February of 2004. She had initially presented to medical attention on September 23, 2004, with a 2-day history of headache, body aches, sore throat (no membrane was present), fever (measured at 103.3<sup>0</sup> F) and no significant adenopathy. A rapid streptococcal antigen test was positive, and the patient was presumptively diagnosed with streptococcal throat infection, treated with benzathine penicillin and discharged home. Because a full throat culture panel had been ordered, tellurite media was used and yielded *C. diphtheriae*. This isolate was forwarded to Centers for Disease Control and Prevention where PCR testing for presence of toxin gene was positive on October 15, 2004, and it was subsequently further characterized as the mitis biotype.

The patient rapidly recovered from her illness without incident. She received a dose of tetanus and diphtheria toxoid-containing (Td) vaccine on October 20, 2004. Of note, a review of the patient's medical record could not identify that she had received any previous doses of Td vaccine.

Four health care providers who had performed oral exams on the index patient and 16 close personal contacts (i.e., those who may have been exposed to respiratory secretions or who were close household contacts) were identified. In conjunction with local public health, the contacts were screened for respiratory symptoms, vaccination histories were reviewed and contacts were vaccinated, if indicated. In addition, nasal and pharyngeal swabs for culture were obtained. Because over 2 weeks had lapsed between the time of potential diphtheria exposure and the time of assessment, CDC recommended these contacts did not need antimicrobial prophylaxis.

The patient's spouse, who is asymptomatic, had a throat culture positive for toxigenic diphtheria, and was treated with benzathine penicillin. He had recently traveled to Haiti in August 2004,

returning on September 6, 2004. All of the other close contacts have also been asymptomatic and all of their cultures for diphtheria are negative. The CDC has confirmed that the areas in Haiti where he traveled have had cases of diphtheria recently reported.

It is **not** clear what role toxigenic diphtheria played in the index patient's symptoms. However, the positive culture from her personal contact underscores the fact that asymptomatic carriage of toxigenic *C. diphtheriae* can occur, and in the U.S. it is more likely to occur in communities in contact with regions of the world where diphtheria is endemic. Although the risk of transmission from asymptomatic carriers is much lower than from ill persons, carriers can transmit diphtheria to other susceptible close contacts.

### **Clinical Manifestations and Etiology**

Diphtheria is an acute bacterial disease caused by toxigenic strains of *C. diphtheriae* and occasionally *C. ulcerans*. It is transmitted through respiratory droplets and direct contact with nasopharyngeal secretions. Diphtheria affects the mucous membranes of the respiratory tract (respiratory diphtheria), the skin (cutaneous diphtheria), and occasionally other sites (eyes, nose, vagina). The incubation period is 2–7 days (range, 1–10 days). If patients are untreated, the infectious period begins at symptom onset and extends through 2 weeks after infection in the majority of patients (but may range up to 6 weeks post onset). If patients are treated with antibiotics, communicability usually lasts less than 4 days

Symptom onset is typically gradual. Early symptoms of respiratory diphtheria include malaise, sore throat, loss of appetite and a low-grade fever. If the larynx is involved, persons may become hoarse and have a barking cough. Within 2-3 days, an adherent, dirty, grey membrane forms over the mucous membrane of the tonsils and/or pharynx. Attempts to remove the membrane cause bleeding. Extensive membrane formation may result in airway obstruction. In severe cases of respiratory diphtheria there is cervical lymphadenopathy and a swollen neck ("bull-neck" appearance). Toxin absorbed from the respiratory tract can cause serious complications, including myocarditis and neuropathies. The case-fatality rate in unimmunized individuals who develop respiratory diphtheria is 5–10%. Cutaneous diphtheria is characterized by a scaling rash or chronic nonhealing ulcers with a dirty gray membrane. Cutaneous and nasal diphtheria are localized infections and rarely associated with systemic toxicity.

### **Epidemiology**

Diphtheria remains a serious disease throughout much of the world. In particular, large outbreaks of diphtheria occurred in the 1990s throughout Russia and the independent countries of the former Soviet Union. Most life-threatening cases occurred in inadequately immunized persons. Travelers to disease-endemic areas are at increased risk for exposure to toxigenic strains of *C. diphtheriae*. Countries with known endemic diphtheria include *Africa* – Algeria, Egypt and the countries in sub-Saharan region; *Americas* – Brazil, Colombia, Dominican Republic, Ecuador, Haiti and Paraguay; *Asia* – Afghanistan, Bangladesh, Bhutan, Cambodia, China, India, Indonesia, Laos, Mongolia, Burma (Myanmar), Nepal, Pakistan, Papua New Guinea, Philippines, Thailand and Vietnam; *Middle East* - Iran, Iraq, Syria and Yemen; *Europe* – Turkey, Albania and all countries of the former Soviet Union.

Diphtheria is uncommon in the United States. Since 2000, only 5 cases of probable or confirmed respiratory diphtheria have been reported to the CDC's National Notifiable Diseases Surveillance System. The most recently reported case in Massachusetts occurred in 1994 in an unvaccinated 4-year-old who died from cardiac and respiratory complications.

## Recommendations:

Routine vaccination is the best preventive measure against diphtheria. Diphtheria and tetanus toxoid-containing and acellular pertussis (DTaP) vaccine should be used in persons < 7 years of age, whereas Td vaccine is the preferred preparation for persons  $\geq$  7 years of age. Tables outlining the routine and accelerated schedules for these vaccines can be found on the next page.

- All patients, particularly those who are **foreign-born**, should have their immunization status assessed to ensure they have received 3-dose primary series of a diphtheria toxoid-containing vaccine. Booster doses of Td should then be administered beginning at age 11-12 years and every 10 years thereafter.
- All travelers to diphtheria endemic areas should be assessed prior to departure and receive a primary series or booster if indicated. Children with any incomplete schedule and adults with fewer than 3 doses should receive as many doses as possible prior to departure, using the accelerated schedules on the next page. This patient and the asymptomatic carrier identified among her contacts underscores the importance of pre-departure consultation and vaccination.
- All children < 7 years of age should receive a routine series of five doses of tetanus and diphtheria toxoid-containing vaccine at ages 2, 4, 6, 15-18 months and 4-6 years.
- All unvaccinated individuals  $\geq$  7 years of age should receive 3 doses of Td vaccine. The second dose is usually given 1-2 months after the 1<sup>st</sup> dose and the 3<sup>rd</sup> dose is given 6 months after the 2<sup>nd</sup> dose.
- Good personal hygiene (which consists of proper hand washing, disposal of used tissues, not sharing eating utensils, etc.) is also important in prevention.
- Clinicians should maintain a higher degree of suspicion for diphtheria among persons with contacts to communities where diphtheria is endemic.
- Suspected diphtheria cases should be reported immediately to MDPH at 617-983-6800 and your local board of health.
  - MDPH has protocols and procedure to assist you with diphtheria diagnosis, treatment and control.
  - Patients with suspected diphtheria will need to have diagnostic specimens collected using the appropriate media and receive antibiotic treatment with penicillin or erythromycin. If respiratory diphtheria is highly suspected, the mainstay of treatment is administration of diphtheria antitoxin (DAT). After their acute illness is resolved, patients should also receive a booster with an age-appropriate diphtheria toxoids-containing vaccine.
  - All close contacts (defined as those who sleep in the same house or who share food, drink, or eating/drinking utensils and healthcare workers exposed to respiratory secretions) should have nasopharyngeal specimens obtained for culture and should also be given antibiotic prophylaxis. Any asymptomatic diphtheria carriers identified should also receive erythromycin or penicillin to eradicate the organism. Td vaccination is recommended for the patient's close contacts if Td has not been administered *within the last 5 years*.

## Vaccine Availability

MDPH distributes DTaP and Td vaccines to **all** providers, both public and private, free-of charge for use in children, adolescents and adults. If you are not enrolled to receive state-supplied vaccines from the Massachusetts Immunization Program, please call our Vaccine Unit at 617-983-6828 to order these vaccines for your patients.

## Schedules for Routine and Accelerated Immunization with Diphtheria and Tetanus Containing Vaccines

### DTaP Schedule for Children < 7 Years of Age<sup>1</sup>

Dose	Vaccine	Recommended Age	Accelerated Schedule
1	DTaP	2 months	≥ 6 weeks of age
2	DTaP	4 months	≥ 4 weeks after 1 <sup>st</sup> dose
3	DTaP	6 months	≥ 4 weeks after 2 <sup>nd</sup> dose
4 <sup>2</sup>	DTaP	15-18 months	≥ 6 months after 3 <sup>rd</sup> dose
5 <sup>2,3</sup>	DTaP	4-6 years	≥ 6 months after 4 <sup>th</sup> dose
Additional Boosters	Td	11 – 12 years of age, if ≥ 5 years since 5 <sup>th</sup> dose, then every 10 years	1 <sup>st</sup> booster ≥ 5 years after the 5 <sup>th</sup> dose, then every 10 years

<sup>1</sup> DTaP and DT should not be given to individuals ≥ 7 years of age.

<sup>2</sup> The 4<sup>th</sup> dose of DTaP may be administered as early as 12 months of age, provided 6 months have elapsed since the 3<sup>rd</sup> dose and the child is unlikely to return at age 15-18 months.

<sup>3</sup> The 5<sup>th</sup> dose of DTaP is not necessary if the 4<sup>th</sup> dose was given on or after the 4<sup>th</sup> birthday.

### Td Schedule for Individuals ≥ 7 Years of Age<sup>1</sup>

Dose	Recommended Schedule	Accelerated Schedule
1	First visit	--
2	1 – 2 months after 1 <sup>st</sup> dose	≥ 4 weeks after 1 <sup>st</sup> dose
3	≥ 6 months after 2 <sup>nd</sup> dose	≥ 6 months after 2 <sup>nd</sup> dose
Additional Boosters	At 11 – 12 years of age and no later than 16 years of age (if it has been ≥ 5 years since last dose), then every 10 yrs. throughout life	--

<sup>1</sup> Td should not be given to individuals < 7 years of age.

### Additional Information about Diphtheria

Information about diphtheria diagnosis, investigation and control can be found in the *Massachusetts Guide to Surveillance and Reporting* at the MDPH website: <http://www.mass.gov/dph>. Additional information about diphtheria can be found on the following CDC website sites:

<http://www.cdc.gov/travel/diseases/dtp.htm> and <http://www.cdc.gov/nip/publications/pink/dip.pdf>